AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1.-16. (Canceled)

17. (Currently Amended) Method for generating transgenic non-human mammalian ~~eukaryotic~~ cells having a modified Rosa26 locus, which method comprises introducing a functional DNA sequence into the Rosa26 locus of non-human mammalian ~~eukaryotic~~ cells to yield transgenic non-human mammalian ~~eukaryotic~~ cells, wherein said functional DNA sequence is a gene expression cassette comprising a gene of interest operatively linked to a promoter**, wherein said promoter is heterologous to the Rosa26 locus,** or **said functional DNA sequence** is a DNA sequence which can be converted into such gene expression cassette.

18. (Currently Amended) The method of claim 17, wherein the functional DNA sequence is introduced into the ~~eukaryotic~~**mammalian** cells by homologous recombination with a targeting vector, the targeting vector comprising said functional DNA sequence flanked by DNA sequences homologous to the Rosa26 ~~locus~~**gene**.

19. (Currently Amended) The method of claim 17, wherein the functional DNA sequence is introduced into the ~~eukaryotic~~**mammalian** cells by site specific recombinase mediated recombination with a recombination vector, the recombination vector comprising said functional DNA sequence flanked by a pair of first recombinase recognition sites (RRSs).

20. – 23. (Canceled)

24. (Currently Amended) The method of claim 17, wherein the non-human mammalian ~~eukaryotic~~ cells are from a rodent.

25. (Previously Presented) The method of claim 24, wherein the rodent is selected from the group consisting of mouse and rat.

26.-27. (Canceled)

28. (Currently Amended) The method of claim 17, wherein the ~~eukaryotic~~**mammalian** cells are selected from the group consisting of primary cells and immortalized cells.

29. (Currently Amended) The method of claim 17, wherein the ~~eukaryotic~~**mammalian** cells are mammalian embryonic stem (ES) cells.

30. (Previously Presented) The method of claim 17, wherein the gene of interest is selected from the group of genes consisting of recombinases, reporter genes, receptors, signaling molecules, transcription factors, pharmaceutically active proteins and peptides, drug target candidates, disease causing gene products and toxins.

31. (Canceled)

32. (Currently Amended) The method of claim [[31]] **17**, wherein the promoter is selected from the group consisting of a constitutive ubiquitous promoter, a constitutive tissue specific promoter, an inducible ubiquitous promoter and an inducible tissue specific promoter.

33. (Currently Amended) The method of claim [[31]] **17**, wherein the promoter is selected from the group consisting of a CAGGS, hCMV, PGK, FABP, Lck, CamKII, CD19, Keratin, Albumin, aP2, Insulin, MCK, MyHC, WAP, Col2A, Mx, tet and Trex promoter.

34. (Currently Amended) The method of claim 17, wherein the functional DNA sequence further comprises one or more additional sequences selected from the group consisting of marker genes, ~~additional~~ recombinase recognition sites, poly A signal and introns.

35. (Previously Presented) The method of claim 18 or 19, wherein the targeting vector or recombination vector further comprises sequences selected from the group consisting of tags for protein detection, enhancers and selection markers.

36. (Previously Presented) The method of claim 18, wherein the DNA sequences homologous to the Rosa26 locus are 0.2 to 20 kB long.

37. (Previously Presented) The method of claim 36, wherein the DNA sequences

homologous to the Rosa26 locus are 1 to 10 kB long.

38. (Currently Amended) The method of claim 36, wherein the ~~eukaryotic~~**mammalian** cells are ~~from~~ mouse **cells** and the DNA sequences homologous to the Rosa26 locus are from the 5' and 3' flanking arm of the mouse Rosa26 ~~locus~~**gene**.

39. (Previously Presented) The method of claim 38, wherein said homologous DNA sequences have the sequences shown in SEQ ID NO:4 and 5.

40. (Currently Amended) The method of claim 36, wherein the ~~eukaryotic~~**mammalian** cells are ~~from~~ mouse **cells**, and the promoter is a CAGGS-promoter.

41. (Currently Amended) The method of claim 36, wherein the targeting vector has the **nucleic acid** sequence shown in SEQ ID NO:7.

42. (Canceled)

43. (Previously Presented) The method of claim 56, wherein the RRS are loxP or FRT sites or variants thereof.

44. (Previously Presented) The method of claim 56, wherein the acceptor DNA comprises a negatively selectable marker gene.

45. (Previously Presented) The method of claim 56, wherein the donor DNA comprises an inactive positive selection marker.

46. (Currently Amended) The method of claim 17, which further comprises one or more of the steps selected from the group consisting of:

(a) isolating the transgenic non-human mammalian ~~eukaryotic~~ cells, and

(b) modifying the functional DNA sequence and isolating transgenic non-human mammalian cells having a modified functional DNA sequence.

47. (Withdrawn) A targeting vector comprising a functional DNA sequence as defined in claim 17.

48. (Currently Amended) A non-human mammalian ~~eukaryotic~~ cell having a

modified Rosa26 locus obtained by the method of claim 17.

49. (Withdrawn) A method for preparing transgenic multi-cell organism having a modified Rosa26 locus which comprises utilizing the method as defined in claim 17.

50. (Withdrawn) The method of claim 49, wherein the transgenic multi-cell organism is a non-human mammal and said method comprises modifying an ES cell.

51. (Withdrawn) The method of claim 49 which further comprises one or more of the steps selected from the group consisting of

(d) injecting ES cells obtained in steps (b) or (c) into blastocysts; and

(e) generating transgenic non-human animals carrying one or more functional genes of interest at the Rosa26 locus.

52. (Withdrawn) A transgenic multi-cell organism and a transgenic non-human mammal obtainable by the method of claim 49, and having an operatively functional gene expression cassette integrated into its Rosa26 locus.

53. (Currently Amended) A method for studying gene functions which comprises (a) providing a biological entity selected from a eukaryotic cell, a transgenic multi-cell **non-human** organism, or a transgenic non-human mammal obtainable utilizing the method of claim 17, (b) expressing the gene of interest and (c) evaluating the function of the gene of interest.

54. (Currently Amended) A method for ~~drug development~~**evaluating the effect of a drug candidate on a gene of interest**, which comprises (a) contacting a drug candidate with a biological entity selected from the eukaryotic cell, a transgenic multi-cell **non-human** organism, or the transgenic non-human mammal obtainable utilizing the method of claim 17, and (b) evaluating the effect of the drug candidate on the gene of interest.

55. (Currently Amended) A method for ~~drug development~~**evaluating the effect of a drug candidate on a gene of interest**, which comprises (a) providing a model of an animal disease comprising a biological entity selected from a eukaryotic cell, a transgenic multi-cell **non-human** organism, or a transgenic non-human mammal obtainable utilizing the method of claim 17, wherein expression of the gene of interest models a disease state of said animal, (b)

contacting the biological entity with a drug candidate and (c) evaluating the effect of the drug candidate on the gene of interest.

56. (Currently Amended) The method of claim 19, which comprises the steps of

(a) introducing into a **non-human** eukaryotic cell an acceptor DNA which integrates into the genome of the eukaryotic cell to yield an acceptor DNA-modified eukaryotic cell, the acceptor DNA comprising two mutally incompatible first RRSs,

(b) introducing a recombination vector ~~as defined in claim 19~~ **comprising a functional DNA sequence** into the acceptor DNA-modified eukaryotic cell, the functional DNA sequence in the recombination vector being donor DNA flanked by two mutually incompatible RRSs that are identical to the two mutually incompatible RRSs in the acceptor DNA; and

(c) introducing into the acceptor DNA-modified eukaryotic cell a recombinase that catalyzes recombination between the RRSs of the acceptor DNA and donor DNA.